CLINICAL SCIENCES

UNMEASURED ANIONS ACCOUNT FOR MOST OF THE METABOLIC ACIDOSIS IN PATIENTS WITH HYPERLACTATEMIA

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PURPOSE: To characterize the different components of metabolic acidosis in patients with hyperlactatemia in order to determine the degree to which lactate is responsible for the acidosis and the relevance that this might have in the outcome of these patients.
METHODS: Arterial blood gas, arterial lactate, Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, phosphate, albumin, and creatinine were measured on admission to make a diagnosis of the acid-base disturbances present. Intensive Care Unit and in-hospital mortality were also recorded.
RESULTS: A total of 58 patients with hyperlactatemia were included. They usually had a mild acidemia (pH 7.31 ± 0.12) and a significantly high Standard Base Deficit (7.6 ± 6.7 mEq/L). In addition to lactate (4.3 ± 2.3 mEq/L), chloride (106.9 ± 9.5 mEq/L) and unmeasured anions (8.6 ± 5.0 mEq/L) accounted for the metabolic acidosis. Unmeasured anions were primarily responsible for the acidosis in both Intensive Care Unit survivors and nonsurvivors (44.7% ± 26.0% and 46.0% ± 17.5%, respectively, P = 0.871). Lactate contributed in similar percentages to the acidosis in both groups (23.0% ± 11.8% and 24.2% ± 9.7% in Intensive Care Unit survivors and nonsurvivors, respectively; P = 0.753). Correlation between Standard Base Deficit and lactate was found only in Intensive Care Unit nonsurvivors (r = 0.662, P < 0.01).
DISCUSSION: Hyperlactatemia is usually accompanied by metabolic acidemia, but lactate is responsible for a minor percentage of the acidosis; unmeasured anions account for most of the acidosis in patients with hyperlactatemia. The percentage of the acidosis due to hyperlactatemia was not relevant in terms of outcome.

KEYWORDS: Hyperlactatemia. Lactic acidosis. Unmeasured anions. Outcome. Critically ill patients.

INTRODUCTION

Since the first definition of hyperlactatemia and lactic acidosis proposed by Huckabee in 1961,[1] many controversies have occurred and different definitions have been proposed in order to determine and separate distinct situations that lead to an altered lactate metabolism. Initially, the terms "hyperlactatemia" or "stress hyperlactatemia" were used for situations in which no concomitant metabolic acidosis (at that time defined as low levels of serum bicarbonate) was present. Increases in serum lactate attributed to an enhanced aerobic glycolytic pathway with a normal pyruvate/lactate ratio were thought to account for the cases of hyperlactatemia without acidosis.

When acidemia and low levels of serum bicarbonate were also present, the term "lactic acidosis" was then used. This condition could occur in the absence or in the presence of tissue hypoperfusion, and physical exam would determine whether there were or were not signs of hemodynamic compromise and circulatory shock.

In 1976, Cohen and Woods[2] abolished the term "hyperlactatemia without acidosis" and classified altered lactate metabolism into lactic acidosis types A and B, using the same previous criteria of presence or absence of tissue dysoxia.

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More recently, the physicochemical approach to acid-base disturbances [3] has supported the idea that there is no reason to separate "hyperlactatemia" and "lactic acidosis" since lactate, as a strong anion, is an acid itself. This modern approach has the great advantage of characterizing the different components of the complex and usually multifactorial metabolic acidosis of critically ill patients.

Standard base deficit (SBD) is frequently used to quantify the degree of metabolic acidosis, and it seems to be a better parameter than bicarbonate, which is highly influenced by the level of pCO_2 and, therefore, by respiratory disturbances. Some authors have defined lactic acidosis as an SBD greater than 2 mEq/L with a lactate component that comprises at least 50% of the SBD.[4]

The aim of this study was to evaluate the SBD and its components in the presence of hyperlactatemia on admission to the intensive care unit (ICU) using the physicochemical approach and to determine to what degree hyperlactatemia was responsible for changes in the SBD. We hypothesized that in a significant number of patients with hyperlactatemia, lactate would not be the major anion responsible for metabolic acidosis and, additionally, that some patients with hyperlactatemia would not actually have metabolic acidosis (defined as an SBD ≥ 2 mEq/L). We also determined whether the percentage of the SBD due to hyperlactatemia was relevant in terms of outcome. Because lactic acidosis seems to be the metabolic acidosis with the poorest prognosis,[4] it is possible that both the absolute levels of lactate and the degree to which lactate contributes to the final SBD are important.

MATERIALS AND METHODS

This study was approved by the local institutional ethics committee. Since all data used here was collected in the process of routine exams performed for all patients that are admitted to our ICU, the requirement for informed written consent was waived.

It is the routine in our 7-bed medical ICU to collect a list of laboratory tests from all patients on admission. This list includes an arterial blood gas determination with simultaneous arterial lactate measurement, Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, phosphate, urea, creatinine, and albumin. From July 2005 until January 2006, all consecutive patients admitted to the ICU and their admission blood gas samples were checked prospectively for hyperlactatemia, defined as an arterial lactate ≥ 2 mEq/L. Patients transferred from or to a different ICU were excluded. In patients with hyperlactatemia, we evaluated the simultaneous arterial pH, standard base deficit (SBD), partial pressure of carbon dioxide (pCO_2), bicarbonate (HCO_3^-), lactate, Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, phosphate, albumin, and creatinine, and we calculated the 4 distinct components of SBD, the apparent strong ion difference (SIDa), the effective strong ion difference (SIDe), and the strong ion gap (SIG) (see below). Age, gender, APACHE II score, ICU mortality, and in-hospital mortality were also recorded for all patients with hyperlactatemia.

Laboratory techniques and measurements

All biochemical variables were simultaneously collected at the time of admission to the ICU. All samples were analyzed in the central laboratory of the Institution. Na^+, K^+, Ca^{2+}, and Cl^- were measured with the use of a direct ion-selective electrode technique, Mg^{2+} by a colorimetric technique, and phosphate with the use of an ultraviolet technique. Albumin was measured with a bromocresol dye colorimetric technique. Arterial blood gas was analyzed and lactate was measured on the OMNI analyzer (Roche Diagnostics System, F. Hoffmann-La Roche Ltd, Basel, Switzerland).

Quantitative physicochemical analysis

According to the contemporary approach to acid-base disturbances proposed by Stewart [3] and then modified by Figge et al,[5] only 3 independent variables can change the blood pH: the strong ion difference (SID), weak acids (mainly phosphate and albumin), and pCO_2. Based on the principles of electroneutrality and conservation of mass, the strong ion difference represents the net balance between positive strong ions (cations) and negative strong ions (anions) according to the following formula (all concentrations in mEq/L):

$$SID = (Na^+ + K^+ + Ca^{2+} + Mg^{2+}) - (Cl^- + lactate^-)$$

Therefore, decreases in the strong ion difference (such as those occurring in hyperchloremia and hyperlactatemia) lead to increases in dissociation of water (to maintain electroneutrality) and a fall in the pH. The opposite happens if the strong ion difference increases. This equation, however, does not take into account the weak acids present in blood; therefore, we call this the apparent strong ion difference (SIDa). The effective strong ion difference (SIDe) is represented by the sum of the charges of the weak acids according to the following equation:

$$SIDe = [(2.46 \times 10^{-8}) * (pCO_2\,(mm\ Hg)/(10^{-pH}))] + [(albumin\ (g/L) * (0.123 \times pH - 0.631)] + [(phosphate\ (mmol/L)) * (0.309 \times pH - 0.469)]$$

In healthy people, no significant amounts of unmeasured anions or lactate are present in the blood. The values of apparent and effective strong ion difference are therefore very close. However, in critically ill patients, both lactate and unmeasured ions are likely to increase. Unmeasured anions, measured by the strong ion gap (SIG), represent the "gap" between apparent and effective strong ion difference as shown in the following formula:

SIG = SIDa – SIDe

In summary, metabolic acidosis, according to the physicochemical theory, can only be the result of decreases in apparent strong ion difference (mainly hyperchloremia and hyperlactatemia), increases in the strong ion gap (unmeasured anions), or increases in weak acids (hyperalbuminemia, which is exceedingly rare, and hyperphosphatemia).

The final result of alkalinizing and acidifying disturbances present in the blood is represented by the SBD, which is the titrable acid in blood,[6] being positive when acidifying disturbances predominate and negative when alkalinizing disturbances are more prevalent. Using a physicochemical analysis, we can separate 4 distinct components of the SBD[7] as follows:

- standard base deficit due to free water (SBDfw), which depends on the concentration of Na^+:

SBDfw = 0.3 x (140 – Na^+ (mEq/L))

- standard base deficit due to chloride (SBDcl), which depends on the concentration of both Na^+ and Cl^-:

SBDcl = (Cl^+ (mEq/L) x (140/Na^+ (mEq/L)) – 102

- standard base deficit due to albumin (SBDalb), which depends on the arterial pH and the concentration of serum albumin:

SBDalb = ((0.148 x pH) – 0.818) x (albumin (g/L) – 45)

- standard base deficit due to lactate and unmeasured anions (SBDua), which corresponds to the rest of the SBD: SBDua = SBD – (SBDfw + SBDcl + SBDalb)

Although there is no consensus about a precise value of the SBD that represents significant metabolic acidosis, we decided to use an arbitrary value of 2 mEq/L, since hypoalbuminemia is an almost universal finding in critically ill patients, contributing a mean value of -5 mEq/L in the final SBD in a recent study.[8] Therefore, even a small positive SBD value, such as 2 mEq/L, could be the consequence of a significant acidifying disturbance.

To calculate the percentage of metabolic acidosis due to hyperlactatemia, we considered the total acidifying elements (SBD acid) as the following (all concentrations in mEq/L):

SBD acid = [lactate] + SBDfw + SBDcl + SIG

We did not use the SBDua in the formula, since it does not discriminate between lactate and unmeasured anions; we preferred to use the strong ion gap,[9] as the equivalent of the unmeasured anions, and lactate, separately. Since hypoalbuminemia is almost invariably present in critically ill patients, SBDalb was not included in the formula (it almost always has an alkalinizing effect). SBDfw and SBDcl were only included in the formula when their sum was positive, ie, when they had an acidifying effect.

The percentage of metabolic acidosis due to lactate (%lactate) and due to the SIG (%SIG) were then determined by the following relationships:

%lactate = lactate / SBD acid
%SIG = SIG / SBD acid

The rest of the metabolic acidosis (not due to lactate or the SIG) was attributed mainly to hyperchloremia.

Statistical analysis

All values were expressed as mean and standard deviation except for 2 variables (Ca^{2+} and creatinine), which required a logarithmic transformation in order to acquire a normal distribution. Their values were expressed as geometric means. The Student t test was used for comparison of continuous parameters, and Pearson's test was used for the correlation analysis. The software SigmaStat for Windows (version 2.0, Copyright$^{\text{ãð}}$ Jandel Corporation) and SPSS for Windows (version 10.0.1, Copyright$^{\text{ãð}}$ SPSS Incorporation) were used for all measurements. A P value less than 0.05 was considered significant.

RESULTS

During the study period, 159 patients were admitted into our ICU, and 152 patients were included in the study; 7 patients were excluded because they came from another ICU or were transferred to another ICU before discharge. Of the 152 patients, we found lactate ≥ 2 mEq/L in 58 patients (38.2%) at admission. The general characteristics of this group of patients are shown in Table 1. Using the physi-

Table 1 - General characteristics of the 58 patients with hyperlactatemia (lactate ≥ 2 mEq/L)

Characteristic	Value (n = 58)
Age – years (mean ± SD)	54 ± 19
Gender - male/female – no. (%)*	30 (52) / 28 (48)
APACHE II score[a] (mean ± SD)	16 ± 8
ICU[b] mortality – no. (%)	16 (28)
Hospital mortality – no. (%)	25 (43)
Diagnosis	
Severe sepsis / septic shock – no. (%)	19 (33)
Post-operative – no. (%)	12 (21)
Respiratory failure – no. (%)	11 (19)
Trauma – no. (%)	5 (9)
Neurologic syndromes[c] – no. (%)	4 (7)
Pancreatitis – no. (%)	2 (3)
Cardiogenic shock – no. (%)	1 (2)
Other – no. (%)	4 (7)

*no. = the number of patients with the characteristic. [a]APACHE II = the acute physiologic and chronic health evaluation score, which ranges from 0 to 72. [b]ICU = intensive care unit. [c]neurologic syndromes including stroke and meningoencephalitis

cochemical approach to analyze the different components of the acid-base disturbances present in these patients (Table 2), we verified that they usually exhibited a mild acidemia (pH 7.31 ± 0.12) and a significant metabolic acidosis (SBD 7.6 ± 6.7 mEq/L). This metabolic acidosis was due to both hyperlactatemia (lactate 4.3 ± 2.3 mEq/L) and hyperchloremia (chloride 107 ± 10 mEq/L), both of which contributed to a decreased apparent strong ion difference (36.3 ± 6.5 mEq/L), and to an increased strong ion gap (8.6 ± 5.0 mEq/L). Serum levels of Na^+, K^+, Ca^{2+}, Mg^{2+}, and phosphate were normal, and low levels of serum albumin (26 ± 8 g/L) attenuated the level of metabolic acidemia. Creatinine was already increased at admission (1.4 ± 2.4 mg/dL). Lactate was 23.3% ± 11.2% of the SBD acid, and the SIG was 45.1% ± 23.9% ($P < 0.001$) (Figure 1). A significant correlation was found between SBD and lactate ($r = 0.322$, $P = 0.01$).

Table 2 - Biochemical variables of the 58 patients with hyperlactatemia (lactate ≥ 2 mEq/L) (mean ± SD)

Variable	Value (n = 58)
pH	7.31 ± 0.12
pCO_2 - mm Hg	35.6 ± 14.3
HCO_3^- - mEq/L	17.7 ± 6.2
SBD* - mEq/L	7.6 ± 6.7
Lactate - mEq/L	4.3 ± 2.3
Na^+ - mEq/L	140 ± 7
K^+ - mEq/L	4.3 ± 0.9
Ca^{2+} [a] - mEq/L	2.3 ± 1.2
Mg^{2+} - mEq/L	1.0 ± 0.3
Cl^- - mEq/L	107 ± 10
Phosphate - mmol/L	1.4 ± 0.5
Albumin - g/L	26 ± 8
SID_a [b] - mEq/L	36.3 ± 6.5
SID_e - mEq/L	27.2 ± 6.4
SIG[c] - mEq/L	8.6 ± 5.0
Creatinine[a] - mg/dL	1.4 ± 2.4
SBD_{fw} - mEq/L	0.0 ± 2.0
SBD_{Cl} - mEq/L	4.8 ± 6.7
SBD_{alb} - mEq/L	-5.0 ± 2.2
SBD_{ua} - mEq/L	7.4 ± 5.9

* SBD = standard base deficit, the respective following abbreviations; denote: FW - free water portion of SBD, Cl - chloride portion of SBD, alb - albumin portion of SBD and ua - unmeasured anions portion of SBD; [a]geometric mean and standard deviation; [b]SID = strong ion difference, and the abbreviations denote: a - apparent SID and e - effective SID; [c]SIG denotes strong ion gap

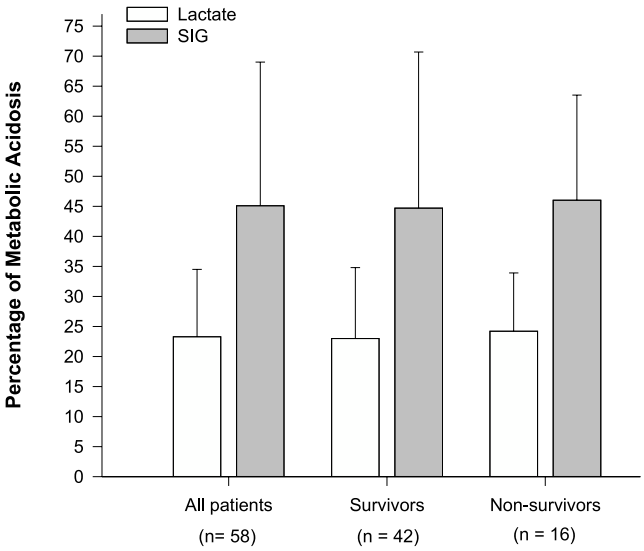

Figure 1 - Percentage of metabolic acidosis due to lactate and the strong ion gap (SIG). Metabolic acidosis was mainly due to the SIG in all groups; the percentage due to lactate was significantly lower than that due to the SIG in all groups ($P < 0.001$). Regarding ICU survivors and nonsurvivors, no difference was found in the percentage of metabolic acidosis due to lactate ($P = 0.753$) or due to the SIG ($P = 0.871$).

We divided the patients grouping into ICU survivors and nonsurvivors, and we then evaluated the same variables described above (Table 3). Both groups were usually acidemic on admission, but nonsurvivors had a tendency to be more acidemic (pH 7.33 ± 0.10 vs 7.26 ± 0.15, $P = 0.05$). Metabolic acidosis was more severe in nonsurvivors (SBD 11.7 ± 7.3 mEq/L vs 6.1 ± 5.8 mEq/L in survivors, $P< 0.01$). The same acidifying variables—hyperlactatemia, hyperchloremia, and increased strong ion gap—contributed to metabolic acidosis in both groups. Of these, only lactate was significantly higher in nonsurvivors (3.8 ± 1.8 vs 5.8 ± 2.9 mEq/L, $P < 0.01$). However, as occurred in the analysis of all patients with hyperlactatemia (Table 2), both survivors and nonsurvivors had a minority of their metabolic acidosis due to lactate. Lactate comprised 23.0% ± 11.8% of the SBD acid in survivors and 24.2% ± 9.7% in nonsurvivors ($P = 0.753$). The SIG comprised 44.7% ± 26.0% of the SBD acid in survivors and 46.0% ± 17.5% in nonsurvivors ($P = 0.871$). The percentage of SBD acid

Table 3 - Comparison between survivors and nonsurvivors (mean ± SD)

Characteristic	Survivors(n = 42)	Nonsurvivors(n = 16)	*P* value
Age - years	55 ± 20	54 ± 20	0.90
APACHE II	14 ± 7	22 ± 6	< 0.01
pH	7.33 ± 0.10	7.26 ± 0.15	0.05
pCO_2 - mm Hg	37.4 ± 14.8	31.0 ± 12.3	0.13
HCO_3^- - mEq/L	19.1 ± 5.7	14.1 ± 6.1	< 0.01
SBD - mEq/L	6.1 ± 5.8	11.7 ± 7.3	< 0.01
Lactate - mEq/L	3.8 ± 1.8	5.8 ± 2.9	< 0.01
Na^+ - mEq/L	140 ± 6	141 ± 8	0.43
K^+ - mEq/L	4.2 ± 0.9	4.3 ± 1.0	0.79
Ca^{2+} [a] - mEq/L	2.3 ± 1.1	2.4 ± 1.3	0.48
Mg^{2+} - mEq/L	1.0 ± 0.3	1.0 ± 0.2	0.64
Cl^- - mEq/L	106 ± 9	108 ± 7	0.39
phosphate - mmol/L	1.3 ± 0.5	1.5 ± 0.7	0.28
Albumin - g/L	28 ± 9	21 ± 5	< 0.01
SID_a [b]- mEq/L	37.3 ± 6.3	33.9 ± 6.6	0.09
SID_e - mEq/L	29.0 ± 5.9	22.2 ± 4.9	< 0.001
SIG[c] - mEq/L	7.9 ± 5.1	10.5 ± 4.0	0.11
Creatinine[a] - mg/dL	1.4 ± 2.3	1.7 ± 2.5	0.45
SBD_{FW}* - mEq/L	0.1 ± 1.8	-0.3 ± 2.4	0.43
SBD_{Cl} - mEq/L	4.2 ± 6.7	6.2 ± 6.7	0.32
SBD_{alb} - mEq/L	-4.6 ± 2.3	-6.2 ± 1.4	0.02
SBD_{ua} - mEq/L	6.3 ± 5.3	10.7 ± 6.5	0.02

* SBD = standard base deficit, the respective following abbreviations denote: FW - free water portion of SBD, Cl - chloride portion of SBD, alb - albumin portion of SBD and ua - unmeasured anions portion of SBD; [a]geometric mean and standard deviation; [b]SID = strong ion difference, and the abbreviations denote: a - apparent SID and e - effective SID; [c]SIG = strong ion gap

due to the strong ion gap was significantly greater than the percentage due to lactate in both survivors and nonsurvivors ($P < 0.001$ for both groups) (Figure 1). All electrolytes were similar in both groups, as was creatinine. Hypoalbuminemia was present in both groups but was greater in nonsurvivors (2.1 ± 0.5 g/dL) than in survivors (2.8 ± 0.8 g/dL) ($P < 0.01$). Correlation between SBD and lactate was absent in survivors ($r = -0.125$, $P = 0.430$) and present in nonsurvivors ($r = 0.662$, $P < 0.01$).

Eight of the 58 patients with hyperlactatemia (13.8%) did not have metabolic acidosis (ie, an SBD > 2 mEq/L). Only 1 died in the ICU. Of the 58 patients with hyperlactatemia, 7 (12.1%) had lactate levels greater than the strong ion gap on admission. All survived until discharge from ICU.

DISCUSSION

Hyperlactatemia is a well established marker of poor outcome in critically ill patients.[10–13] However, interpretation of high levels of lactate is a challenge to intensivists, since its etiology and pathophysiology is not always clear. Until recently, it was common to use the terms "hyperlactatemia" and "lactic acidosis" interchangeably and as synonyms of "tissue hypoperfusion;" however, this is not always the case.[14] Although we have shown in our study that patients with hyperlactatemia usually presented with metabolic acidemia, and that at admission, both lactate and the SBD were significantly different between ICU survivors and nonsurvivors, lactate was not primarily responsible for the acidemia; it was rather, the unmeasured anions that were primarily responsible. The etiology and pathophysiology of increased levels of unmeasured anions is even more obscure than that of hyperlactatemia. They are thought to increase in many distinct situations such as renal and hepatic impairment,[15] tissue hypoperfusion,[16] and endotoxemia.[17]

Controversy exists regarding the relevance that unmeasured anions have in the outcome of critically ill patients.[18–20] In our study, the strong ion gap was not different between survivors and nonsurvivors at admission, but this could have been due to the small sample size. In a larger study, Cusack et al[18] also failed to find a significant difference in the strong ion gap between survivors and nonsurvivors. Similarly to our study, they found a relevant difference in the SBDua between survivors and nonsurvivors. Although both the strong ion gap and SBDua are variables used to quantify unmeasured anions, SBDua includes lactate and the strong ion gap does not. This could explain the fact that in both studies, SBDua was different in survivors vs nonsurvivors, while the strong ion gap was not. Kellum suggested that the use of gelatins as resuscitation fluids may interfere in the prognostic relevance of unmeasured anions.[21] Neither do our ICU, or our Emergency Department use this type of colloid; rather, we use crystalloids in the resuscitation of our patients and only rarely colloids.

We found unmeasured anions to be the most important acidifying variable in patients with hyperlactatemia, even greater than lactate itself. If we use the definition of lactic acidosis proposed by Gunnerson et al[4] (lactate accounting for more than 50% of the metabolic acidosis), most of patients with hyperlactatemia actually did not have lactic acidosis. Although these authors found lactate to be primarily responsible for metabolic acidosis in more patients than were unmeasured anions, they selected only patients with suspected lactic acidosis with an SBD higher than 2 mEq/L. We found 13.8% of the patients with hyperlactatemia to have an SBD lower than 2 mEq/L. Additionally, in their study, not all values were collected at the same time on the day of admission, and they studied a distinct population. This could explain at least in part the differences between their findings and ours.

Most studies in critically ill patients have found a poor correlation between the SBD and lactate.[22–24] This could be explained by the fact that lactate only represents a small percentage of the SBD in most patients, in agreement with the finding of our study. On the other hand, we found that although the percentage of metabolic acidosis due to lactate was similar between survivors and nonsurvivors with hyperlactatemia, a significant correlation between lactate and the SBD was only present in nonsurvivors. The most feasible explanation would be that nonsurvivors had higher levels of lactate, which could have resulted in a correlation between the two variables. However, we had previously found a correlation between lactate and the SBD only in ICU nonsurvivors even when comparing groups with similar levels of lactate.[25] According to the theory of unreversed ATP hydrolysis proposed by Zilva,[26] hyperlactatemia in anaerobic conditions is followed by metabolic acidosis due to the accumulation of protons that were produced in the glycolytic pathway but not used in the oxidative metabolism. At that time, lactate was not considered an acid. However, if the Zilva theory is true, depending on the origin of hyperlactatemia (aerobic or anaerobic), the same level of lactate could lead to distinctly different degrees of metabolic acidosis. It is probable that in the group of ICU nonsurvivors, more patients had hyperlactatemia due to tissue hypoperfusion and anaerobiosis. This could lead to the presence of a significant correlation between lactate and the SBD in only this group of patients.

Our study had some limitations. Since we used only a specific group of critically ill patients (those presenting hyperlactatemia at admission to the ICU) during a short observation period, our sample size was small; some absence of difference between groups could be due to this fact. We also had a heterogenous population of critically ill patients, so it is not easy to arrive at conclusions regarding any specific group of patients, such as for instance septic patients.

Although largely used to define metabolic acidosis, the SBD is the sum of both acidifying and alkalinizing variables. Therefore, normal values for the SBD may result when significant acidifying disturbances including hyperlactatemia occur concomitantly with significant alkalinizing disturbances such as hypoalbuminemia. We found a small proportion of patients with hyperlactatemia having normal or even low values for the SBD, and we used the term "hyperlactatemia without acidosis" for these patients, but this may not be appropriate or may even be paradoxical.

The fact is that current literature does not have very precise and accurate definitions for "metabolic acidosis" and "lactic acidosis." A large variability between definitions makes the comparison between studies very difficult. Gunnerson et al[4] defined "lactic acidosis" as lactate accounting for more than 50% of the SBD. However, they did not clearly define how they calculated this percentage. Since, as we have already noted, the SBD includes alkalinizing variables, it would be more appropriate to calculate this percentage by selecting only the acidifying variables (the SBD acid in our study). The use of the total SBD may overestimate the percentage of acidosis due to lactate.

Finally, all the data in this study were limited to the day of admission. Evolutive changes in lactate and the SBD are certainly very important in the outcome of these patients. However, the aim of this study was to check for the prevalence of anions other than lactate on admission of patients with hyperlactatemia and not to evaluate the evolution of these anions during ICU stay. Our findings show that although very relevant in terms of prognosis, lactate is only the tip of a much larger iceberg predominantly comprised of unmeasured anions.

COMPETING INTERESTS

The authors declare that they have no competing interests.

RESUMO

Maciel AT, Park M. Ânions não mensuráveis são responsáveis pela maior parte da acidose metabólica de pacientes com hiperlactatemia. Clinics. 2007;62(1):55-62.

OBJETIVO: Caracterizar os diferentes componentes da acidose metabólica de pacientes com hiperlactatemia de modo a verificar o quanto o lactato é responsável pela acidose e a relevância que isso possa ter no prognóstico desses pacientes.

MÉTODOS: Gasometria arterial com dosagem de lactato, Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, fosfato, albumina e creatinina séricas foram coletados no momento da admissão para fazer o diagnóstico dos possíveis distúrbios ácido-básicos presentes. Mortalidade na UTI e mortalidade hospitalar foram avaliadas.

RESULTADOS: Um total de 58 pacientes com hiperlactatemia foram incluídos. Eles tinham na média uma acidemia leve (pH 7.31 ± 0.12) e o déficit de base significativamente elevado (7.6 ± 6.7 mEq/L). Além do lactato (4.3 ± 2.3 mEq/L), o cloro (106.9 ± 9.5 mEq/L) e os ânions não mensuráveis (8.6 ± 5.0 mEq/L) contribuíram para a acidose metabólica. Os ânions não mensuráveis foram responsáveis pela maior parcela da acidose tanto nos pacientes que tiveram alta da UTI como nos que faleceram (44.7 ± 26.0 % e 46.0 ± 17.5 %, respectivamente, p= 0.871). O lactato contribuiu em percentagens semelhantes para a acidose em ambos os grupos (23.0 ± 11.8 % nos sobreviventes e 24.2 ± 9.7 % nos óbitos, p= 0.753). Correlação entre o déficit de base e o lactato somente foi encontrada nos óbitos ($r = 0.662$, $p < 0.01$).

DISCUSSÃO: Hiperlactatemia é comumente acompanhada de acidemia metabólica, porém o lactato corresponde a uma parcela minoritária da acidose; ânions não mensuráveis contribuem com a maior parte da carga ácida em pacientes hiperlactatêmicos. O percentual da acidose devido à hiperlactatemia não foi relevante em termos de prognóstico.

UNITERMOS: Hiperlactatemia. Acidose láctica. Ânions não mensuráveis. Prognóstico. Pacientes críticos.

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